

Study Protocol

Cross cultural validation of the Italian version of the Bt-DUX: A subjective measure of health related quality of life in patients who underwent surgery for lower extremity malignant bone tumour.

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1. Background

Malignant bone tumours like osteosarcoma and Ewing sarcoma mostly appear at the teenage years and in the long bones of the lower extremity. The survival rates for children and adolescents with lower-extremity sarcoma have improved remarkably over the past decades. As result of the improved life expectancy, there has been a growing interest in functional outcome and Quality of Life (QoL) after surgery. Most of the studies on the outcome of surgery so far were mainly focused on basic daily activities or have used generic instruments for QoL. With the usage of these instruments a number of relevant issues, such as the patient's valuation of the cosmetic, functional and emotional impact of the disease and its surgical treatment, are not specifically taken into account.

These latter dimensions are included in a recently developed questionnaire DUX for bone tumours in children and adolescents (Bt-DUX). The Bt-DUX questionnaire was constructed as a disease specific questionnaire, modelled upon the generic DUX 25 QoL questionnaire (short version of the Dutch Children TNO-AZL Quality of Life Questionnaire / DUCATQOL). The DUX 25 has been used in studies among siblings of paediatric cancer patients, children with celiac disease, juvenile chronic arthritis, malignant bone tumours and healthy peers and proved to be internally consistent and reproducible. The scores on the Bt-DUX reflect patients' personal impact; their individual values for cosmetic, social, emotional and functional aspects of their life after the surgery. The Dutch version of the Bt-DUX was found to be a practically applicable instrument with a good internal consistency and validity and appeared to have added value regarding existing measures of quality of life in patients undergoing surgery for malignant bone tumours of the lower extremity (1). The Bt-DUX has been translated into the English language and this Bt-DUX translation has also proven to be a valid disease-specific instrument for evaluating QoL of adolescents with lower extremity bone cancer (2). The Bt-DUX has been used as disease specific QoL instrument in cross sectional and prospective studies among patients after bone cancer surgery and has given a valuable addition to the generic and age specific QoL measures (3,4). To examine the validity of the Bt-DUX within bigger and/or international studies it's from importance to translate the instrument in other languages and validate the instrument in other cultures / populations. Therefore we'd like to translate and cross-cultural validate the Bt-DUX in the Italian language.

2. The study

Purpose: The purpose of the presented study is to translate the English Bt-DUX (Bt-DUX-Eng) questionnaire into the Italian language and then examine the validity of the Italian version of the Bt-DUX (Bt-DUX-It).

Design: Cross sectional study among patients of the Istituto Ortopedico Rizzoli, Bologna, Italy. A survey consisting of different QoL questionnaires will be executed.

2.1 *Method:*

The study will be undertaken in two phases:

- Adaptation into the target language.
- Validation of the translated Bt-DUX

2.1.1 Adaptation into the target language

The method used is a well established process set down by Beaton et al, (2). It comprises five stages:

- Initial translation
- Synthesis of these translations
- Back translation
- Expert committee assessment
- Field testing

Stage I: Initial translation

The first stage in adaptation is the forward translation. At least two forward translations should be made of the instrument from the English Bt-DUX into the Italian language. In this way, the translations can be compared, and discrepancies which may reflect ambiguous wording in the original language, or discrepancies in how a word is translated can be identified. Poorer wording

choices can then be discussed and resolved as the best translation between the translators. The two independent translations are produced by bilingual translators who have Italian as their mother tongue. Translations into the first language of the translator are more likely to accurately reflect the nuances of that language. The two translators should have different profiles or backgrounds to ensure the best possible translation.

Translator 1: Should be knowledgeable about the type of concepts the questionnaire being translated addresses (e.g. cancer / children). Translator 1 adaptations will be aimed at equivalency from a more clinical perspective, and may produce a translation that is a more reliable equivalence to the original from a measurement perspective.

Translator 2: The other translator should neither be aware nor be informed of the concepts being quantified, and preferably have no medical/clinical background. As the so-called “naive” translator, he or she is more likely to detect the more subtle differences in meaning of the original than the first translator. Translator 2 should not be influenced by an academic goal, and offer a translation that reflects the language used by the lay population. This second translation will often highlight more ambiguous meanings in the original questionnaire than is found in the first translation (3).

The two translators each produce a written report of their translation. Comments are included to highlight challenging phrases or uncertainties along with the rationale for final choices. The questions, response options and any instructions are all translated using the same process.

Stage II: Synthesis of the translations

To produce a synthesis of the two translations, a third, unbiased person is added to the team. The role of this person is to serve as a mediator in discussions of translation differences, and to produce a written documentation of the process. Working from the original questionnaire as well as the first translator’s version (T1) and the second translator’s (T2), a synthesis of these translations is produced, resulting in one common translation (T-12). A written report documenting the process, each issue addressed, and how it was resolved is completed. It is

important that all issues be resolved by consensus rather than one person compromising their feelings.

Stage III: Back-translation:

Working from the T-12 version of the questionnaire, and totally blind to the original version, the questionnaire is then translated back into the original language. This is a process of validity checking to make sure the translated version accurately reflects the item content of the original version. The back translation process often magnifies unclear wording in the translations. However, agreement between the back translation and the original source version does not guarantee a satisfactory forward translation version (T-12), as an incorrect, but consistent translation could occur (4). Back translation is only one type of validity check, and is best at highlighting gross inconsistencies or conceptual errors in the translation. As with forward translations, two back-translations are considered a minimum. The back-translations (BT1 and BT2) are produced by two bilingual persons with English as their mother tongue. The two translators should neither be aware nor be informed of the concepts explored, and preferably without medical background. The main reasons for this are to avoid information bias and to elicit unexpected meanings of the items in the translated questionnaire (T-12) (3,4), thus increase the likelihood of “highlighting the imperfections” (4).

Stage IV: Expert Committee

The composition of the Expert Committee is crucial to achieving cross-cultural equivalence of the translated instrument. The minimum composition of the Expert Committee should include:

- A methodologist
- A health professional
- All the translators (both forward and backward)
- The translation synthesis recorder

The original developers of the questionnaire should be in close contact with the Expert Committee during this part of the process to respond to questions and provide input.

The Expert Committee's role is to consolidate all the versions and components of the questionnaire and all translated versions (T1, T2, T12, BT1, BT2), and develop the final version of the questionnaire for field testing. The Committee will review all of the translations and reach a consensus on any discrepancy found. Corresponding written reports explaining the rationale of each decision at earlier stages of the process should also be available.

Critical decisions are made by the Expert Committee in finalizing the translated instrument, and full written documentation should be made of the issues and rationale for all decisions about any of the components. Decisions will need to be made by this Committee to achieve equivalence between the source and target version in four areas set out below (3):

- **Linguistic equivalence**

Do the words mean the same thing? Are there multiple meanings to a given item? Are there grammatical difficulties in the translation?

- **Idiomatic equivalence**

Colloquialisms, or idioms, are difficult to translate. The committee may have to formulate an equivalent expression in the target version.

- **Experiential equivalence**

Items seeking to capture and experience of daily life often vary in different countries and cultures. In some instances, a given task may simply not be experienced in the target culture, even if it is translatable. To address this situation, a questionnaire item addressing a similar action or intent in the target culture would need to be identified to replace the original item.

- **Conceptual equivalence**

Often words hold different conceptual meaning between cultures. For instance, the meaning of “seeing your family as much as you would like” would differ between cultures based on the concept of what defines “family” (i.e., nuclear versus extended family).

The Expert Committee will need to examine the source and back-translated questionnaires for all of these types of equivalence items. Consensus among Committee members should be reached on all items, and if necessary, the translation/back translation process repeated to clarify how another wording of an item would work. The advantage of having all translators present on the Committee is that discrepancies or changes in wording could be done immediately. The final questionnaire

should be able to be understood by the equivalent of a 12-year-old (roughly a grade six level of reading), as this is the general recommended reading level for questionnaires.

2.1.2 Validation of the Italian Bt-DUX

The validity of the Bt-DUX-It will be evaluated in accordance with the validation of the original Dutch Bt-DUX and Bt-DUX-Eng by computing the internal consistency, construct and discriminant validity. Therefore different questionnaires at the domains of Quality of Life and Functional Limitations will be employed.

Patients: All patients who underwent a surgical intervention due to a malignant bone tumour in the leg will be identified through hospital records. Patients are eligible if they're aged between 15 and 25 years at the time of the selection, if the time since surgery is ranged between 12 and 60 months, if the malignant bone tumour (osteosarcoma or Ewing's sarcoma) was located around the hip or the knee and the surgical intervention consisted of limb sparing or ablative surgery. Patients will be excluded if other medical conditions limit their physical activities.

Instruments:

Bt-DUX (1). The disease specific Bt-DUX relates to the patient's subjective feeling about a specific aspect, using abstract faces (smiley's) as answer categories. The expressions from very happy to sad (score 1-5) form a five-point Likert scale. The Bt-DUX consists of 20 questions which cover the domains social, emotional, cosmetrical and physical functioning. Single item scores were recoded and computed into raw total and domain scores. These raw scores were converted into total and domain scores, ranging from 0-100, with the highest scores indicating better QoL .

EORTC QLQ C-30. The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life Questionnaire is a well-validated instrument that assesses health-related quality at life (HRQOL) in cancer patients. It is used in cancer clinical trials in Europe, Canada, and the United States, and has demonstrated high reliability and validity in different groups of cancer patients. The 30-item EORTC QLQ-C30 questionnaire is composed of scales that evaluate physical functioning and role functioning, as well as emotional, social, and cognitive functioning

and global QOL. Three symptom scales measure fatigue, pain, and emesis, while six single items assess financial impact and physical symptoms such as dyspnoea, sleep disturbance, appetite, diarrhoea, and constipation. The time frame is the past week. The questions are formatted with either yes or no answers, or by using four-answer categories that range from 1, not at all, to 4, very much. The two questions on general health and global QOL are to be answered on a numbered visual-analogue scale from 1 to 7.

The Toronto Extremity Salvage Score (TESS) (7), a validated and reliable disease-specific measure developed to evaluate physical disability in patients treated for extremity sarcoma. The self-administered questionnaire includes 30 items on activity limitations in daily life, such as restrictions in body movement, mobility, self-care and performance of daily tasks and routine. The degree of physical disability is rated from 0 (not possible) to 5 (without any problem). The raw score is converted to a score ranged from 0 to 100 points, with higher scores indicating no functional limitations.

Statistical analysis:

Descriptive statistics will be used for the patient's clinical demographic and outcome measures. Bar statistics will be viewed to evaluate the distribution of the total and domain scores. Internal consistency of the Bt-DUX-It will be determined by calculating Cronbach's α and by computing the correlation between the four domain scores and the total Bt-DUX-It score (domain-total correlation). A Cronbach's α value of 0.85 will be considered as good (9). In order to evaluate the preconceived domain structure of the Bt-DUX, an analysis of the item-domain correlation and the Cronbach's α of the four domains will be performed.

Construct validity of the Bt-DUX-It will be determined by calculating Spearman correlation coefficients between the Bt-DUX-It and the measures of quality of life (EORTC QLQ-C30) and functional ability domain (TESS). Discriminate validity will be evaluated by the ability of the Bt-DUX-It to discriminate between patients with worse and better functional status than the median value of the outcome measure.

3. Endpoints:

At least 50 patients need to be included to determine the validity of the Italian version of the Bt-DUX. Final goal of the study is to establish the Bt-DUX as a disease specific instrument to evaluate quality of life in children and young adults after surgery due to a malignant bone tumour of the leg.

4. Ethics and Regulatory

4.1 Ethical approval

Approval for the developmental work on the Dutch version of the Bt-DUX was obtained from the Medical Ethical Committee of the Leiden University Medical Centre. It is envisaged that the validation of the Italian Bt-DUX will be appropriate to the Italian regulations. Each patient involved in the study should complete a written consent form.

This protocol, the informed consent form and all the necessary relevant information related to the study must be submitted to the Ethics Committee for evaluation and must be approved before the start of the study. The study will be conducted in accordance with international standards ISO 14:155, with the Good Clinical Practice and with the national laws in force.

It is the responsibility of the investigator to inform the local Ethics Committee if any changes are made to the protocol or if any severe adverse effects occur. The investigator stores all correspondence with the Ethics regarding the study.

4.2 Patient Information and Informed Consent

Prior to patient enrollment the Investigator will provide explanation about the study in detail, handout the Patient Information and Informed Consent Form. He will also be available for any question the patient has about the study. Further he will explain alternative treatment methods and that the patients' data will be protected. Finally a written consent of the patient will be obtained prior to patient enrolment by signing the Patient Consent Form.

The permission for the use of anonymized patient data for medical and scientific purposes is given as part of the Patient Consent Form.

5. Publication of Results

The main investigator undertakes to produce the final report, publish all the data collected as described in the protocol and to ensure that the data is reported responsibly and consistently. In particular, the publication of the data deriving from this study will take place regardless of the results obtained. The transmission or dissemination of data, through scientific publications and / or presentations in congresses conferences and seminars, will take place exclusively following the merely statistical elaboration of the same, or in any case in an absolutely anonymous form.

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